Wave 3
Communications Supplement

6-Amino-m-Cresol

Olive

Phenyl-Substituted Methicones

ReReviews - Lanolin; BHA

Zanthoxylum piperitum

Resource Document: Nitrosation

EXPERT PANEL MEETING
JUNE 12-13, 2023

Personal Care Products Council
Committed to Safety, Quality & Innovation

Memorandum

TO: Bart Heldreth, Ph.D.
Executive Director - Cosmetic Ingredient Review

FROM: Alexandra Kowcz, MS, MBA
Industry Liaison to the CIR Expert Panel

DATE: June 5, 2023

SUBJECT: Draft Tentative Amended Report: Amended Safety Assessment of 6-Amino-m-Cresol as Used in Cosmetics (draft prepared for the June 2023 meeting)

The Personal Care Products Council respectfully submits the following comments on the draft tentative amended report, Amended Safety Assessment of 6-Amino-m-Cresol as Used in Cosmetics.

Dermal Absorption - The value "100 mg/cm^2" is a dose. The SCCS opinion called it "Area Dose". The CIR report says: "The area dosed was 100 mg/cm^2." which suggest it is an area. It could be called the dose per unit area. Please revise the CIR report to make it clear that it is a dose.

Short-Term, old report summary – The paragraph describing the 4-week rat study from the original report could be more concise. For example, this paragraph states: "Water consumption was also increased." and "Highly significant results were reported for increased water consumption…" It also states: "decreased iron in females" and "Iron was significantly reduced in females".

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TO: Bart Heldreth, Ph.D.
Executive Director - Cosmetic Ingredient Review

FROM: Alexandra Kowcz, MS, MBA
Industry Liaison to the CIR Expert Panel

DATE: June 5, 2023

SUBJECT: Draft Tentative Report: Safety Assessment of *Olea europaea* (Olive)-Derived Ingredients as Used in Cosmetics (draft prepared for the June 2023 meeting)

The Personal Care Products Council respectfully submits the following comments on the draft tentative report, Safety Assessment of *Olea europaea* (Olive)-Derived Ingredients as Used in Cosmetics.

Method of Manufacture – The following sentence is unnecessary for this report: "It is unknown if the general methodologies of the processing of Olea europaea (olive)-derived ingredients described below apply to cosmetic ingredient manufacturing." Information in the Dictionary and information from suppliers of cosmetic ingredients apply to cosmetic ingredient manufacturing. It is not always clear if method of manufacture in published papers apply to cosmetic ingredients, but the papers often say the purpose of the ingredient which could be stated in the CIR report. For example, the title of references 11 and 15 indicate use in food. These are the only two references in this section not specifically related to cosmetic ingredients – and the purpose of the ingredients is noted in the titles.

Composition and Impurities, Olea Europaea (Olive) Sap Extract – Please delete "metabolites" in "Constituents of olive sap metabolites include…."

Short-Term and Subchronic – Please state that the concentrations of olive leaf extract (up to 0.9%) given to rats in the 42-day study were dietary concentrations. Units of mg/kg bw/day should be called "dose" not "concentration".

Dermal Irritation and Sensitization – In the text, please include the number of subjects used in the dermal irritation studies.

Summary – Please correct: "produced not dermal sensitization" ("not" should be "no")

Discussion – Where are the data on skin lightening effects? If the statement on skin lightening is referring to the Dictionary stating skin lightening function for the extracts of fruit and leaves, the Discussion should be specific and not suggest that there are data regarding skin lightening effects.

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TO: Bart Heldreth, Ph.D.
Executive Director - Cosmetic Ingredient Review

FROM: Alexandra Kowcz, MS, MBA
Industry Liaison to the CIR Expert Panel

DATE: June 5, 2023

SUBJECT: Draft Tentative Report: Safety Assessment of Phenyl-Substituted Methicones as Used in Cosmetics (draft prepared for the June 2023 meeting)

The Personal Care Products Council respectfully submits the following comments on the draft tentative report, Safety Assessment of Phenyl-Substituted Methicones as Used in Cosmetics.

Key Issues

Now that three CAS numbers (70131-69-0, 18758-91-3, 18876-34-1) are no longer associated with the INCI name Phenyl Trimethicone in the Dictionary, it would have been helpful if in addition to the name Phenyl Trimethicone, the CAS number 70131-69-0 or the silsesquioxane name (e.g., Polyphenylsilsesquioxane) would also have been stated with the studies on this material. This would have made it easier for the Expert Panel to identify the studies on this material and to remove those studies from the report if the Expert Panel determines that they are not appropriate.

The title of reference 27 includes the CAS number 63148-58-3. In the Dictionary, this CAS number is associated with Phenyl Methicone. The 10-day inhalation study cited to reference 27 indicates that Phenyl Trimethicone was tested. Is this correct?

Additional Considerations

ADME – What was measured in the oral study? The description says “test article”, but the results say “siloxane as silicon”. If they were measuring silicon, “test article” should be changed to “silicon”.

Acute; Summary – Please correct: “in an acute oral toxicity evaluating” (add “study”)

DART, old report summary – The summary of information from the original report states: "Untreated animals served as controls." and "while untreated animals served as controls". Only one of these statements is necessary.

DART, Oral; Summary – Please correct: "mean ration live births/litter size" ("ration" should be "ratio")

DART, Oral - What type of oil was used as the vehicle in the 4-week study in male Wistar rats?

Exposure Assessment; Summary – The Summary identifies the exposure assessment as "Australian"; the Exposure Assessment section does not say "Australian". The Summary should not have more information than the section.

Summary – Please correct "an ampoule formulations" (if more than one formulation was tested delete "an"; if one formulation was tested, delete "s" on formulations)

Summary and/or Discussion – As the Expert Panel considered it to be an important study, please mention the 4-week inhalation study on Phenyl Trimethicone from the original report.

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TO: Bart Heldreth, Ph.D.
Executive Director - Cosmetic Ingredient Review

FROM: Alexandra Kowcz, MS, MBA
Industry Liaison to the CIR Expert Panel

DATE: June 5, 2023

SUBJECT: June 2023 Re-Reviews (drafts prepared for the June 2023 meeting)

The Personal Care Products Council (PCPC) respectfully submits the following comments on the re-reviews considered during the June 2023 meeting of the Expert Panel for Cosmetic Ingredient Safety.

Lanolin

Memo – In the memo, it would have been helpful to note the FDA product categories in which the high concentrations were used. The 40% product is for nail cream and lotion, while the 2002 maximum of 37% is for body and hand products. Therefore, although the concentration may be higher in the most recent survey, the exposure to a body and hand product is higher than exposure to a nail cream and lotion.

Lanolin/Lanolin Alcohol, Clinical Studies, Different from Existing Data? Column – What is the basis for the suggestion that sensitization rates have increased since the original report? In this table, 3 studies show increases, and 2 studies show decreases in sensitization rates. In his announcement of Lanolin as allergen of the year, Dr. Silverberg suggested that sensitization rates seem to be stable.

Clinical studies, Elmobdy et al. 2023 – 1020 should be corrected to 2020

BHA

Toxicity, first 3 studies – The first three studies from the ECHA dossier are all cited to RTECs. All indicate that the dose was a total dose which is not stated in the summary table. This should be made clear if a new CIR report on BHA is prepared. The total dose in the monkey study was actually 14,000 mg/kg bw not 15,000 as stated in the table.

Toxicity, Sun et al. 2020 – It is not clear what happened to the rats fed the high fat diet.

Toxicity, Jeong et al. 2005 – Were there any effects at 10 mg/kg/day?

No Comments
Polyquaternium-11
Octoxynols
Benzaldehyde

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Executive Director - Cosmetic Ingredient Review

FROM: Alexandra Kowcz, MS, MBA
Industry Liaison to the CIR Expert Panel

DATE: June 5, 2023

SUBJECT: Draft Tentative Report: Safety Assessment of *Zanthoxylum piperitum*-Derived Ingredients as Used in Cosmetics (draft prepared for the June 2023 meeting)

The Personal Care Products Council respectfully submits the following comments on the draft tentative report, Safety Assessment of *Zanthoxylum piperitum*-Derived Ingredients as Used in Cosmetics.

Definition and Plant Identification – Because it is not stated in the definition, it would be helpful to note that the chemical class for Zanthoxylum Piperitum Oil is essential oils and waters, to make it clear that this is not a triglyceride oil (chemical class fats and oils).

Composition/Impurities – Please revise: "Sanshoamide, a component from the fresh unripe fruits of *Zanthoxylum piperitum*, has also been reported as a component." It is not necessary to say that sanshoamide is a component twice in the same sentence.

Composition/Impurities, Zanthoxylum Piperitum Fruit Extract – The title of reference 12 calls it an "oil". The method of manufacture "pericarp steam distillate" is also consistent with how essential oils are made. Perhaps this study should be moved under the Zanthoxylum Piperitum Oil subheading.

Cosmetic Use; Summary – Please state the FDA cosmetic product categories for which the maximum use concentration of 0.0022% was reported.

ADME; Summary – It states that: hydroxy-α-sanshool "had the highest plasma concentration". Is this compared to other components of *Zanthoxylum piperitum*, or to components of the other plants included in the mixture?

Anti-Carcinogenicity studies; Cytotoxicity – Since the studies in both sections are about cell death in cancer cell lines, they should be presented in the same section. How did the study authors of reference 23 determine it was apoptosis rather than another type of cell death?

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TO: Bart Heldreth, Ph.D.
Executive Director - Cosmetic Ingredient Review

FROM: Alexandra Kowcz, MS, MBA
Industry Liaison to the CIR Expert Panel

DATE: June 5, 2023

SUBJECT: Draft Resource Document: N-Nitrosation and the Safety Evaluation of Cosmetic Ingredients (draft prepared for the June 2023 meeting)

The Personal Care Products Council respectfully submits the following comments on the draft resource document, N-Nitrosation and the Safety Evaluation of Cosmetic Ingredients.

After comments from the Expert Panel for Cosmetic Ingredient Safety have been incorporated into the Nitrosation resource document, we request that the document be posted on CIR's website for a 60-day comment period before it is reviewed again by the Expert Panel.

Background – As indicated in the document, the formation of N-nitrosamines is a formulation issue. As the Expert Panel for Cosmetic Ingredient Safety assesses the safety of ingredients not formulations, the last sentence of the background should be revised. Rather than saying: "how the Panel assesses and determines the potential risks linked to N-nitrosation in cosmetic formulations" to "how the Panel identifies ingredients that have the potential to form N-nitrosamines in formulation."

Conclusion – Please revise "consider strategies that prevent the formation of N-nitrosamines" to "use strategies that prevent the formation of N-nitrosamines."

Reference 24 – Please include the date (2009) of the Cosmetics Europe technical guidance document.